UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/591,789	06/12/2000	John J. Machalonis	7760-012	5233

20583 7590 02/15/2002

PENNIE AND EDMONDS
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 100362711

EXAMINER
PARKIN, JEFFREY S

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 02/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/591,789	Applicant(s) Machalonis, J. J., et al.
	Examiner Jeffrey S. Parkin, Ph.D.	Art Unit 1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *30 Nov 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above, claim(s) *1-6 and 8-23* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *7, 24, and 25* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

Detailed Office Action

Status of the Claims

1. Applicants' election with traverse of Group II (claims 6, 7, 24, and 25), as it pertains to the peptide having SEQ ID NO.: 1, in Paper No. 4 is acknowledged. Because applicant did not distinctly and specifically point out the purported errors in the restriction requirement, as it pertained to the identification of Groups I-VII, this portion of the election has been treated as an election without traverse (refer to M.P.E.P. § 818.03(a)). However, applicants did traverse the restriction requirement specifying that each individual peptide constitutes an independent and distinct invention. Applicants requested that this portion of the restriction be modified to a species election. Applicants contend that it would not constitute a serious burden to examine fifteen different peptides at once. This argument is not deemed to be persuasive. Each of the identified peptides has a different primary amino acid sequence with different attendant physical and biochemical properties and activities. Moreover, the peptides do not share any common structural or functional motifs. Accordingly, each peptide will have to be searched individually. Contrary to applicants' assertion, a search directed toward all the peptides clearly would constitute an undue burden on both the Examiner and Scientific and Technical Information Center (STIC) which must process such requests. Applicants' arguments have been thoroughly considered but are not deemed persuasive for the reasons set forth *supra* and in the original restriction requirement. **The requirement is still deemed to be proper and is therefore made FINAL.** Claims 1-6 and 8-23 are withdrawn from further consideration by the examiner, pursuant to 37 C.F.R. § 1.142(b), as being drawn to a

non-elected invention.[1]

Abstract

2. This application does not contain an abstract of the disclosure as required by 37 C.F.R. § 1.72(b). An abstract on a separate sheet is required.

Claim Objections

3. Claims 7, 24, and 25 are objected to because of the following informalities: the claims fail to reflect the restriction set forth in the last Office action and applicants' election set forth in paper no. 4. The claims should be amended to properly reflect the elected invention (i.e., A method to increase ... comprising administering an effective amount of a peptide having SEQ ID NO.: 1, wherein ...). Claim 25 contains the term "interleutkin-4" which should read --interleukin-4--. Appropriate correction is required.

35 U.S.C. § 112, First Paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 7, 24, and 25 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to

---

[1] Applicants are advised that the elected peptide having SEQ ID NO.: 1 is not listed in claim 6. Accordingly, claim 6 has been withdrawn as being directed toward a non-elected invention.

make and/or use the invention. The claims are directed toward a method for increasing T_H1 cytokine production while decreasing T_H2 cytokine production through the administration of a peptide having SEQ ID NO.: 1. The purpose of this modulation is to prevent and/or treat cardiovascular disease, allergic disorders, solid tumors, and the progression to AIDS in an HIV-positive patient (first paragraph, p.1). The invention appears to be predicated upon the assumption that these various pathologies can be treated by shifting the immune state of a patient from that of a T_H2 state, which is generally associated with phagocyte-independent immune responses (i.e., IgE production, IgG production, mast cell activation and differentiation), to one of a T_H1 state, which is generally associated with phagocyte-dependent immune responses (i.e., delayed-type hypersensitivity, production of opsonizing antibodies, production of complement-fixing antibodies).

The legal considerations that govern enablement determinations pertaining to undue experimentation are disclosed in *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988) and *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:
1) The disclosure fails to provide adequate guidance pertaining to the molecular determinants modulating the favorable immunological properties and activities of the claimed peptide. The claimed invention involves the administration of a T-cell receptor (TCR)

peptide to the patient. The TCR is a heterodimeric cell surface protein comprising an α and β polypeptide that is normally involved in a number of immunological responses such as antigen recognition (Davis and Chien, 1999). The TCR recognizes antigenic peptides presented in the context of MHC class I or II. Each α and β subunit is glycosylated and has a molecular weight of 40,000-50,000. TCRs are quite diverse and share structural similarities with immunoglobulins including variable, constant, and joining regions. Thus, they are quite complex molecules. However, the disclosure fails to provide any guidance pertaining to the location of the TCR peptide within the context of the larger receptor. Thus, it is not readily manifest how the administration of this peptide will modulate the immune response in favor of T_H1-type responses. The disclosure fails to provide any guidance pertaining to the biochemical and immunological activities of the claimed peptide (i.e., agonist or antagonist). For instance, does the peptide act by inhibiting TCR interactions on $CD4^+$ T-lymphocytes or does it function in some other manner. How will the skilled artisan keep the peptide from interfering with all normal TCR interactions on both $CD4^+$ and $CD8^+$ T-lymphocytes? What will preclude the patient from developing an immune response against the peptide of interest thereby leading to aberrant immunological activity (i.e., down-modulation of TCR-mediated immune responses)? 2) The disclosure fails to teach that modulating T_H1/T_H2 cytokine levels will have any ameliorative or therapeutic effect in cardiovascular disease, allergic disorders, solid tumors, or the progression to AIDS. The correlates of protective immunity for many disorders remain to be elucidated. Moreover, many pathogens and disease states fail to elicit a simple T_H1 or T_H2 phenotype (Graziosi *et al.*, 1994; Maggi *et al.*, 1994; Romagnani *et al.*, 1994; Shearer and Clerici, 1992). For instance, it is not clear what type of immune responses will protect against solid tumors, allergic disorders, cardiovascular disease, or the progression to

AIDS. In some situations, both humoral and cell-mediated immune responses may be required. Thus, the interplay between "T_H1/T_H2" cytokine responses may not be so simple. In fact, what is more likely to required, is a balance between the two responses to favorably eliminate tumors and HIV. It is not readily manifest how the peptide of interest would facilitate the treatment of cardiovascular disease. For instance, would the peptide be capable of inducing immune responses that remove plaque from clogged arteries? What type of allergic disorders could the peptide of interest prevent or treat? Absent sufficient guidance from the disclosure, the skilled artisan has been extended an undue invitation to further experimentation.

3) The disclosure fails to provide any working embodiments. The disclosure fails to provide any relevant models of tumor progression, cardiovascular disease, allergic disorders, or HIV infection. The disclosure fails to provide any data involving the claimed peptide demonstrating that it can effectively treat tumor development, AIDS progression, cardiovascular disease, or sundry allergic disorders. The development of any given therapeutic is a difficult process involving testing of the peptide or compound of interest in *in vitro* tissue culture assays, *in vivo* animal models, and finally in preliminary clinical studies. Only be performing such studies can the skilled artisan reasonably conclude that such compounds will be efficacious (Öberg and Vrang, 1990; Gait and Karn, 1995; Yarchoan and Broder, 1992). However, the disclosure fails to provide suitable evidence in support of the claimed activity of the TCR peptide.

4) As discussed *supra*, the prior art is unpredictable and teaches that the development of efficacious treatments for cardiovascular disease, allergic disorders, solid tumors, and antivirals is an arduous and often unsuccessful undertaking (Graziosi *et al.*, 1994; Maggi *et al.*, 1994; Romagnani *et al.*, 1994; Shearer and Clerici,

1992; Öberg and Vrang, 1990; Gait and Karn, 1995; Yarchoan and Broder, 1992). Moreover, the complexity of the TCR and the various roles it plays in T-cell signaling make it difficult to identify and predict which compounds will prove useful as therapeutic agents (Evavold *et al.*, 1993; Madrenas *et al.*, 1996). Perusal of the disclosure fails to provide any evidence that would lead the skilled artisan to conclude otherwise.

5) The claims are of considerable breadth and remain unsupported by the disclosure. The claims encompass the treatment of any solid tumor, any cardiovascular disorder, any allergic disorder, and the progression to AIDS. As noted above, the disclosure fails to provide support for any of these claims. The first paragraph of § 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification. *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970). *In re Vaeck*, 20 U.S.P.Q.2d 1438 (C.A.F.C. 1991). *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). Clearly the inventors have not met their obligation under this section. Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation to practice the claimed invention.

Correspondence

6. Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Official communications should be directed toward one of the following Group 1600 fax numbers: (703) 308-4242 or (703) 305-3014. Informal communications may be submitted directly to the Examiner through the following fax number: (703) 308-4426. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

7. Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (703) 308-2227. The examiner can normally be reached Monday through Thursday from

8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, James Housel or Laurie Scheiner, can be reached at (703) 308-4027 or (703) 308-1122, respectively. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

09 February, 2002